150. The immunogenic composition according to claim 145, wherein said deletion results in the expression of a truncated *nef* gene product.

Sub. E1

151. The immunogenic composition according to claim 145, wherein said deletion comprises at least 10 nucleotides.

Dec'd

152. The immunogenic composition according to claim 145, wherein said isolate of HIV-1 is selected from the group of viruses consisting of V94101706, V941031169, and V95031022.

REMARKS

In response to the Final Action dated September 26, 2001 and the Advisory Action dated April 10, 2002, and further in connection with the filing of the Request for Continued Examination pursuant to 37 C.F.R. §1.114, Applicants respectfully submit the instant amendment which, when considered in view of the following remarks, is deemed to place the present application in condition for allowance. Favorable consideration of all pending claims is respectfully requested.

Claims 49-50, 66-67, 85 and 120-136 are presently pending in the application. Claims 49-50, 66-67 and 120-126 are drawn to methods for vaccinating an individual against the development of AIDS or AIDS-related diseases by administering to the individual a non-pathogenic isolate of HIV-1. Claims 85 and 127-136 are drawn to vaccine compositions comprising a non-pathogenic isolate of HIV-1. The non-pathogenic isolate of HIV-1 recited in the instant claims is characterized as comprising a genomic deletion in the region corresponding to nucleotides 9281-9438 of the *nef* gene and U3 long terminal repeat (which region comprises the nucleotide sequence coding for amino acids 166-206 of the *nef* protein).

In the Final Action dated September 26, 2001, claims 49-50, 66-67, 85 and 120-136 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling support. Claim 85 is rejected under 35 U.S.C. §112, second paragraph as allegedly referring to features of non-elected subject matter. Claims 122, 124, 129 and 134 are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite.

In raising the rejection under 35 U.S.C. §112, first paragraph, the Examiner alleges that the specification fails to provide adequate guidance concerning the selection of allelic variants of *nef* or any other HIV viral gene that would be non-pathogenic. The Examiner points out that the SBBC patients described in the specification were all infected with the same parental virus having a deletion in the *nef*/LTR region. The Examiner also contends that the specification fails to demonstrate that the instantly claimed HIV-1 vaccines employing *nef* deletion variants would mount an efficacious humoral or cellular immune response resulting in the *prevention or treatment* of HIV infection.

In response to the Final Action, Applicants previously amended the claims and referred the Examiner to two articles, Dyer et al. (*J. Virol. 73*: 436-443, 1999) and Kent et al. article (*Journal of Virology* 75:11930-19934, 2001), as support of the enablement of the claimed subject matter. Dyer et al. report that the Sydney Blood Bank Cohort (SBBC) strain of HIV-1 induced strong anti-HIV-1 cytotoxic T-cell responses in four out of seven recipients. Kent et al. describe certain attenuated SIV isolates (having a genomic deletion analogous to HIV-1_{nl43} referred to in the present application) that protected recipient monkeys against infection by wild-type SIV.

In the Advisory Action issued April 10, 2002, the Examiner states that Applicants' response has overcome the rejections under 35 U.S.C. §112, second paragraph. However, the

Examiner maintains that the claimed subject matter is not enabled. Specifically, the Examiner contends that the Kent et al. reference was published well after the filing date of the instant application and fails to demonstrate that the claimed invention was enabled at the time of filing. In addition, the Examiner alleges that Kent et al. employed a construct that differs significantly from that disclosed and currently claimed by Applicants.

Applicants respectfully submit that the law does not preclude submission of post-filing data which demonstrate that the claimed invention functions in the manner described. Contrary to the Examiner's allegation, it is observed that the attenuated SIV isolates employed by Kent et al. are analogous to the non-pathogenic HIV-1 isolates taught in the present specification – that is, the attenuated SIV isolates all contain a deletion in the 3' nef-LTR region (two of the four SIV isolates contain an additional deletion in the 5' LTR region). In addition, the techniques used by Kent et al. in determining the protective effects of the attenuated SIV isolates, including those for measuring the level of plasma SIV RNA and the level of CD4+ lymphocytes techniques, were all available to those skilled in the art at the time the present application was filed. Kent et al. demonstrate that attenuated SIV constructs, which mimick the HIV-1 constructs disclosed in the present application having a deletion in the *nef*/LTR region, protected monkeys from challenge from infections by wild type virus. Thus, Kent et al. provide evidence of the effectiveness of the claimed vaccine compositions containing a non-pathogenic HIV-1 isolate and methods of vaccination. Applicants respectfully submit that the weight of such evidence should not be affected by the fact that it was first disclosed after the filing of the instant application.

Applicants respectfully submit that both Dyer et al. and Kent et al. provide further support for the enablement of the claimed vaccine compositions and vaccination methods. In

addition, it would be unrealistic and it is not required under the law for Applicants to obtain human clinical data in order to satisfy the enablement requirement.

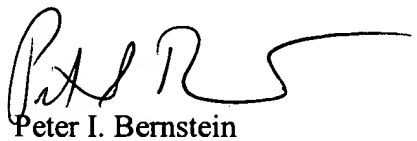
In view of the foregoing, Applicants respectfully submit that claims 49-50, 66-67, 85 and 120-136 are fully enabled by the specification under 35 U.S.C. §112, first paragraph. Favorable consideration of these claims is respectfully requested.

By way of the instant amendment, Applicants have also added claims directed to methods of inducing an immune response against HIV-1 (claims 137-144) and to immunogenic compositions (claims 145-152). Support for these claims is found throughout the specification, e.g., at page 6, line 5; page 16, line 7-10; page 86, line 25 through page 87, line 10. No new matter is introduced.

Attached hereto is a marked-up version of the changes made to the claims by the instant amendment, captioned "**Version with Markings to Show Changes Made.**"

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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